



03-29-03

1634.

Attorney Docket No. 5470-401

PATENT

## IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Stafford et al.  
Application No.: 10/573,131  
Filed: April 18, 2006

Confirmation No.: 4529  
Group Art Unit: 1634  
Examiner: J. Sitton

For: *METHODS AND COMPOSITIONS FOR THE CORRELATION OF SINGLE  
NUCLEOTIDE POLYMORPHISMS IN THE VITAMIN K EPOXIDE REDUCTASE GENE AND  
WARFARIN DOSAGE*

Date: March 28, 2007

Mail Stop Amendment  
Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

**SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT  
PURSUANT TO 37 C.F.R. §1.97(b)**

Sir:

Attached is a list of documents, together with a copy of any listed foreign patent document and/or non-patent literature. A copy of any listed U.S. patent and/or U.S. patent application publication is not provided herewith in accordance with the amendment by the U.S. Patent and Trademark Office to 37 C.F.R. § 1.98(a)(2)(ii) effective October 21, 2004.

This Information Disclosure Statement is submitted in accordance with 37 C.F.R. § 1.97(b), within three months of the filing date of the above-referenced application or before the mailing of a first Office Action on the merits, whichever event occurs last. Therefore, no fee is believed due. However, the Commissioner is hereby authorized to charge any deficiency or credit any overpayment to Deposit Account No. 50-0220.

It is requested that these documents be considered by the Examiner and officially made of record in accordance with the provisions of 37 C.F.R. § 1.56 and Section 609 of the MPEP.

Respectfully submitted,

Mary L. Miller  
Registration No. 39,303

Myers Bigel Sibley & Sajovec, P.A.  
P. O. Box 37428  
Raleigh, North Carolina 27627  
Telephone: (919) 854-1400  
Facsimile: (919) 854-1401  
Customer No. 20792

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Tracy Wallace

# INFORMATION DISCLOSURE STATEMENT BY APPLICANT

(use as many sheets as necessary)

Sheet 1 of 7



## Complete if Known

Application Number	10/573,131
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First Named Inventor	Darrel W. Stafford
Group Art Unit	1634
Examiner Name	J. Sitton
Attorney Docket Number	5470-401

## U.S. PATENTS AND PATENT PUBLICATIONS

Examiner Initials*	Cite No.	U.S. Patent Document		Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY
		Number	Kind Code (if known)		
	1.	4,736,866		Leder et al.	4/12/1998
	2.	4,816,397		Boss et al.	3/28/1989
	3.	4,816,567		Cabilly et al.	3/28/1989
	4.	5,547,835		Koster et al.	8/20/1996
	5.	5,583,278		Alt. et al.	12/10/1996
	6.	5,625,122		Mak	4/29/1997
	7.	5,698,765		Mak	12/26/1997
	8.	5,750,825		Yazaki et al.	5/12/1998
	9.	6,043,031		Koster et al.	3/28/2000
	10.	6,492,115		Guida et al.	12/10/2002
	11.	US 2005/0164367		Fenge et al.	7/28/2005
	12.	US 2006/0166239		Chen et al.	7/27/2006
	13.	US 2006/0194284		Oldenburg et al.	8/31/2006
	14.	US 2007/0009950		Stafford et al.	1/11/2007

## FOREIGN PATENT DOCUMENTS

Examiner Initials*	Cite No.	Foreign Patent Document			Name of Patentee or Applicant of Cited Document	Date of Publication of Cited Document MM-DD-YYYY	Translation
		Office	Number	Kind Code (if known)			
	15.	DE	196 25 049		Becker et al.	1/2/1998	No
	16.	EP	0 368 684	B1	Medical Research Council	5/16/1990	
	17.	EP	0 127 839	B1	Texas A & M University System	12/12/1984	
	18.	EP	0 154 133	B1	Genentech, Inc.	9/11/1985	
	19.	EP	0 549 721	B1	The Texas A & M University System	7/07/1993	
	20.	PCT	WO 88/01649		Genex Corporation	3/10/1988	
	21.	PCT	WO 93/06213		Medical Research Council	4/01/1993	
	22.	PCT	WO 95/34679		The Gov't of the United States	12/21/1995	
	23.	PCT	WO 97/49802		Becker et al.	12/31/1997	Abstract only
	24.	PCT	WO 98/24884		Genpharm International	6/11/1998	
	25.	PCT	WO 99/43003		Micron Technology, Inc.	8/26/1999	
	26.	PCT	WO 00/03015		Incyte Pharmaceuticals	1/20/2000	
	27.	PCT	WO 2005/030039		Stafford et al.	4/07/2005	
	28.	PCT	WO 2006/044686		Rieder et al.	4/27/2006	
	29.	PCT	WO 2006/101474		Stafford et al.	9/28/2006	

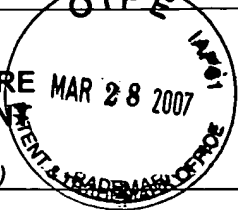
## OTHER NON PATENT DOCUMENTS

Examiner Initials*	Cite No.	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published	T
	30.	Altschul et al. "Gapped BLAST and PSI-BLAST: a new generation of protein database search programs" <i>Nucleic Acids Research</i> 25(17):3389-3402 (1997)	
	31.	Bandyopadhyay et al. "γ-Glutamyl carboxylation: An extracellular posttranslational modification that antedates the divergence of mollusks, arthropods, and chordates" <i>PNAS</i> 99(3):1264-1269 (2002)	
	32.	Bell et al. "Warfarin and the inhibition of vitamin K activity by an oxide metabolite" <i>Nature</i> 237:32-33 (1972)	
	33.	Berkner et al. "The Vitamin K-Dependent Carboxylase" <i>J. Nutr.</i> 130:1877-1880 (2000)	
	34.	Blann et al. "Racial background is a determinant of average warfarin dose required to maintain the INR between 2.0 and 3.0" <i>Br J Haematol.</i> 107(1):207-209 (1999)	

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Date Considered

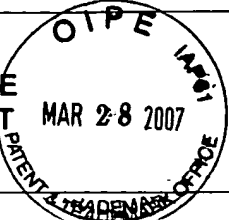
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<b>INFORMATION DISCLOSURE STATEMENT BY APPLICANT</b> (use as many sheets as necessary) Sheet 2 of 7				<b>Complete if Known</b>	
		Application Number		10/573,131	
		Filing Date		April 18, 2006	
		First Named Inventor		Darrel W. Stafford	
		Group Art Unit		1634	
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35.	Boneh et al. "Hereditary Deficiency of Vitamin K-Dependent Coagulation Factors With Skeletal Abnormalities" <i>American Journal of Medical Genetics</i> 65:241-243 (1996)	
36.	Brenner et al. "A Missense Mutation in $\gamma$ -Glutamyl Carboxylase Gene Causes Combined Deficiency of All Vitamin K-Dependent Blood Coagulation Factors" <i>Blood</i> 92(12):4554-4559 (1998)	
37.	Cain et al. "Assembly of the Warfarin-sensitive Vitamin K 2,3-Epoxy Reductase Enzyme Complex in the Endoplasmic Reticulum Membrane" <i>The Journal of Biological Chemistry</i> 272(46):29068-29075 (1997)	
38.	Cain et al. "Warfarin Resistance Is Associated with a Protein Component of the Vitamin K 2,3-Epoxy Reductase Enzyme Complex in Rat Liver" <i>Thromb Haemost</i> 80:128-33 (1998)	
39.	Camire et al. "Enhanced $\gamma$ -Carboxylation of Recombinant Factor X Using a Chimeric Construct Containing the Prothrombin Propeptide" <i>Biochemistry</i> 39:14322-14329 (2000)	
40.	Carter et al. "Prothrombin G20210A is a bifunctional gene polymorphism" <i>Thromb Haemost.</i> 87(5):846-853(2002)	
41.	Chu et al. "A Mutation in the Propeptide of Factor IX Leads to Warfarin Sensitivity by a Novel Mechanism" <i>J. Clin. Invest.</i> 98(7):1619-1625 (1996)	
42.	Chu et al. "Purified vitamin K epoxide reductase alone is sufficient for conversion of vitamin K epoxide to vitamin K and vitamin K to vitamin KH <sub>2</sub> " <i>PNAS</i> 103(51):19308-19313 (2006)	
43.	Copy of International Search Report for PCT/EP2006/000734, dated May 11, 2006	
44.	Crawford et al. "Haplotype Diversity across 100 Candidate Genes for Inflammation, Lipid Metabolism, and Blood Pressure Regulation in Two Populations" <i>Am J. Hum. Genet.</i> 74:610-622 (2004)	
45.	Derian et al. "Inhibitors of 2-Ketoglutarate-dependent Dioxygenases Block Aspartyl $\beta$ -Hydroxylation of Recombinant Human Factor IX in Several Mammalian Expression Systems" <i>The Journal of Biological Chemistry</i> 264(12):6615-6618 (1989)	
46.	Dockal et al. "Five recombinant fragments of human serum albumin-tools for the characterization of the warfarin binding site" <i>Protein Sci.</i> 9:1455-1465 (2000)	
47.	Dockal et al. "The Three Recombinant Domains of Human Serum Albumin" <i>The Journal of Biological Chemistry</i> 274(41):29303-29310 (1999)	
48.	Drysdale et al. "Complex promoter and coding region $\beta$ 2-adrenergic receptor haplotypes alter receptor expression and predict <i>in vivo</i> responsiveness" <i>PNAS</i> 97(19):10483-10488 (2000)	
49.	Esmon et al. "The Functional Significance of Vitamin K Action" <i>The Journal of Biological Chemistry</i> 250(11):4095-4099 (1975)	
50.	Esmon et al. "The New Carboxylation Reaction" <i>The Journal of Biological Chemistry</i> 250(12):4744-4748 (1975)	
51.	Fasco et al. "Formation of Hydroxyvitamin K by Vitamin K Epoxide Reductase of Warfarin-resistant Rats" <i>The Journal of Biological Chemistry</i> 258(7):4372-4380 (1983)	
52.	Fasco et al. "Warfarin Inhibition of Vitamin K 2,3-Epoxy Reductase in Rat Liver Microsomes" <i>Biochemistry</i> 22:5655-5660 (1983)	
53.	Furie et al. "The Molecular Basis of Blood Coagulation" <i>Cell</i> 53:505-518 (1988)	
54.	Furie et al. "Vitamin K-Dependent Biosynthesis of $\gamma$ -Carboxyglutamic Acid" <i>Blood</i> 93(6):1798-1808 (1999)	
55.	Gage et al. "Adverse Outcomes and Predictors of Underuse of Antithrombic Therapy in Medicare Beneficiaries with Chronic Atrial Fibrillation" <i>Stroke</i> 31:822-827 (2000)	
56.	Gage et al. "Use of pharmacogenetics and clinical factors to predict the maintenance dose of warfarin" <i>Thromb Haemost.</i> 91(1):87-94 (2004)	
57.	GenBank Accession No. AC135050, <i>Homo sapiens</i> chromosome 16 clone RP11-196G11, complete sequence, October 5, 2002	
58.	GenBank Accession No. AK002742, <i>Mus musculus</i> adult male kidney cDNA, clone:0610033K05, July 10, 2000	
59.	GenBank Accession No. AK013996, <i>Mus musculus</i> 13 days embryo head cDNA, clone:3110005B16, July 10, 2000	
60.	GenBank Accession No. AV003686, <i>Mus musculus</i> C57BL/8J kidney <i>Mus musculus</i> cDNA, clone:0610033K05, Unpublished 1999	

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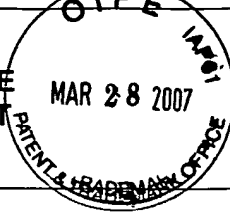
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	61.	GenBank Accession No. AV162712, <i>Mus musculus</i> head C57BL/6 13-dat embryo <i>Mus Musculus</i> cDNA, clone:3110005B16, Unpublished 1999	
	62.	GenBank Accession No. AY587020, <i>Homo sapiens</i> vitamin K epoxide reductase complex, March 31, 2004	
	63.	GenBank Accession No. BC000828, <i>Homo sapiens</i> vitamin K epoxide reductase complex, CDNA clone IMAGE:3455200, November 15, 2000	
	64.	GenBank Accession No. BC002911.1, <i>Homo sapiens</i> , clone MGC:11276, February 5, 2001	
	65.	GenBank Accession No. BC002911.2, <i>Homo sapiens</i> vitamin K epoxide reductase complex, clone MGC:11276, February 5, 2001	
	66.	GenBank Accession No. BC027734, <i>Homo sapiens</i> vitamin K-epoxide reductase complex, clone MGC:29720, April 8, 2002	
	67.	GenBank Accession No. BY703248, adult male kidney <i>Mus musculus</i> , clone 0610033K05, December 16, 2002	
	68.	GenBank Accession No. NG_005631, <i>Homo sapiens</i> vitamin K epoxide reductase complex, LOC441241, derived from AC073210.8, <i>Homo sapiens</i> BAC clone RP11-460N20, complete sequence, June 10, 2000	
	69.	GenBank Accession No. NM_178600, <i>Mus musculus</i> vitamin K epoxide reductase complex, Vkorc1, derived from AK003237.1, <i>Mus musculus</i> 18-day embryo whole body cDNA, clone:1110001K05, July 10, 2000 and CD774813.1, NIH_BMAP_MHI <i>Mus musculus</i> cDNA clone, July 2, 2003	
	70.	GenBank Accession No. NM_178600.2, <i>Mus musculus</i> vitamin K epoxide reductase complex, Vkorc1, March 16, 2004	
	71.	GenBank Accession No. NM_024006.1, <i>Homo sapiens</i> hypothetical protein, IMAGE 3455200, October 5, 2003	
	72.	GenBank Accession No. NM_024006.4, <i>Homo sapiens</i> vitamin K epoxide reductase complex, VKORC1, March 11, 2007	
	73.	GenBank Accession No. NM_203335, <i>Rattus norvegicus</i> vitamin K epoxide reductase complex, Vkorc1, derived from CB314647.1, NICHDRr_Pit1 <i>Rattus norvegicus</i> cDNA clone, IMAGE:6890244, March 3, 2003, AY423047.1, <i>Rattus norvegicus</i> vitamin K epoxide reductase complex subunit 1(Vkorc1) mRNA, complete cds, Sept. 25, 2003 and AW253787.1, UI-R-BJ0-acz-d-05-0-UI.s1 UI-R-BJ0 <i>Rattus norvegicus</i> cDNA clone, December 17, 1999	
	74.	GenBank Accession No. NM_206807, <i>Gallus gallus</i> vitamin K epoxide reductase complex, VKORC1, derived from AW355622, <i>Gallus gallus</i> cDNA clone pftlc.pk003.d10, June 23, 2006, and BU114821.1, CHSEQCHL14 <i>Gallus gallus</i> cDNA clone ChEST105p15, November 25, 2002	
	75.	GenBank Accession No. NM_206824, <i>Homo sapiens</i> vitamin K epoxide reductase complex, VKORC1, derived from BI822140.1, 603039843F1 NIH_MGC_115 <i>Homo sapiens</i> cDNA clone IMAGE:5180554, October 4, 2001, AK129513.1, <i>Homo sapiens</i> cDNA FLJ26002 fis, clone DMC07743, July 31, 2003 and CD249837.1, NIH_MGC_172 <i>Homo sapiens</i> cDNA, Unpublished 1999	
	76.	GenBank Accession No. NP_848715, vitamin K epoxide reductase complex, subunit 1 [ <i>Mus musculus</i> ], derived from AK003237.1, <i>Mus musculus</i> 18-day embryo whole body cDNA, clone:1110001K05, July 10, 2000 and CD774813.1, NIH_BMAP_MHI <i>Mus musculus</i> cDNA clone, July 2, 2003	
	77.	Swiss-Prot Accession No. Q9CRC0, Vitamin K epoxide reductase complex subunit 1 (Vitamin K1 2,3-epoxide reductase subunit 1), Jun 1, 2001	
	78.	Goldsmith et al. "Studies on a Family with Combined Functional Deficiencies of Vitamin K-dependent Coagulation Factors" <i>J. Clin. Invest.</i> 69:1253-1260 (1982)	
	79.	Gossen et al. "Inducible gene expression systems for higher eukaryotic cells" <i>Current Opinion in Biotechnology</i> 5:516-520 (1994)	
	80.	Greaves et al. "Heritable Resistance to Warfarin in Rats" <i>Nature</i> 215:877-878 (1967)	
	81.	Guenther et al. "Co-purification of Microsomal Epoxide Hydrolase with the Warfarin-Sensitive Vitamin K1 Oxide Reductase of the Vitamin K Cycle" <i>Biochemical Pharmacology</i> 55:169-175 (1998)	
	82.	Hacker et al. "Lack of association between an interleukin-1 receptor antagonist gene polymorphism and ulcerative colitis" <i>Gut</i> 40:623-627 (1997)	
	83.	Hallgren et al. "Carboxylase overexpression effects full carboxylation but poor release and secretion of factor IX: implications for the release of vitamin K-dependent proteins" <i>Biochemistry</i> 41(50):15045-55 (2002)	

Examiner Signature		Date Considered	
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Sheet	4 of 7						

84.	Higashi et al. "Association between CYP2C9 genetic variants and anticoagulation-related outcomes during warfarin therapy" <i>JAMA</i> 287(13):1690-1698 (2002)	
85.	Hirsh et al. "Oral Anticoagulants: Mechanism of Action, Clinical Effectiveness, and Optimal Therapeutic Range" <i>Chest</i> 119:8s-21s (2001)	
86.	Houben et al. "Osteocalcin binds tightly to the $\gamma$ -glutamylcarboxylase at a site distinct from that of the other known vitamin K-dependent proteins" <i>Biochem. J.</i> 341:265-269 (1999)	
87.	Huisse et al. "Mechanism of the Abnormal Vitamin K-dependent $\gamma$ -Carboxylation Process in Human Hepatocellular Carcinomas" <i>Cancer</i> 74:1533-41 (1994)	
88.	Jackson et al. "Identification of a consensus motif for retention of transmembrane proteins in the endoplasmic reticulum" <i>The EMBO Journal</i> 9(10):3153-3162 (1990)	
89.	Johnson et al. "Characterization of a Variant Prothrombin in a Patient Congenitally Deficient in Factors II, VII, IX, and X" <i>British Journal of Haematology</i> 44:461-469 (1980)	
90.	Kaminsky et al. "Correlation of human cytochrome P450C substrate specificities with primary structure: warfarin as a probe" <i>Mol Pharmacol.</i> 43(2):234-239 (1993)	
91.	Kaminsky et al. "Human hepatic cytochrome P-450 composition as probed by <i>in vitro</i> microsomal metabolism of warfarin" <i>Drug Metab Dispos.</i> 12(4):470-477 (1984)	
92.	Kaufman et al. "Expression, Purification, and Characterization of Recombinant $\gamma$ -Carboxylated Factor IX Synthesized in Chinese Hamster Ovary Cells" <i>The Journal of Biological Chemistry</i> 261(21):9622-9628 (1986)	
93.	Kohn et al. "Genomic assignment of the warfarin resistance locus, <i>Rw</i> , in the rat" <i>Mammalian Genome</i> 10:696-698 (1999)	
94.	Kozak et al. "An analysis of 5'-noncoding sequences from 699 vertebrate messenger RNAs" <i>Nucleic Acids Research</i> 15(20):8125-8148 (1987)	
95.	Laupacis et al. "Antithrombotic therapy in atrial fibrillation" <i>Chest</i> 114:579s-589s (1998)	
96.	Lee et al. "Glucocorticoids regulate expression of dihydrofolate reductase cDNA in mouse mammary tumour virus chimaeric plasmids" <i>Nature</i> 294:228-232 (1981)	
97.	Lesko et al. "Translation of pharmacogenomics and pharmacogenetics: a regulatory perspective" <i>Nat Rev Drug Discov.</i> 3(9):763-769 (2004)	
98.	Li et al. "Identification of a <i>Drosophila</i> Vitamin K-dependent $\gamma$ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 275:18291-18296 (2000)	
99.	Lin et al. "Binding of the Factor IX $\gamma$ -Carboxyglutamic Acid Domain to the Vitamin K-dependent $\gamma$ -Glutamyl Carboxylase Active Site Induces an Allosteric Effect That May Ensure Processive Carboxylation and Regulate the Release of Carboxylated Product" <i>The Journal of Biological Chemistry</i> 279(8):6560-6566 (2004)	
100.	Lin et al. "The Putative Vitamin K-dependent $\gamma$ -Glutamyl Carboxylase Internal Propeptide Appears to Be the Propeptide Binding Site" <i>The Journal of Biological Chemistry</i> 277(32):28584-28591 (2002)	
101.	Malhotra et al. "The Kinetics of Activation of Normal and $\gamma$ -Carboxyglutamic Acid-deficient Prothrombins" <i>The Journal of Biological Chemistry</i> 260(1):279-287 (1985)	
102.	Manfioletti et al. "The Protein Encoded by a Growth Arrest-Specific Gene ( <i>gas6</i> ) Is a New Member of the Vitamin K-Dependent Proteins Related to Protein S, a Negative Coregulator in the Blood Coagulation Cascade" <i>Molecular and Cellular Biology</i> 13(8):4976-4985 (1993)	
103.	Mann et al. "Cofactor proteins in the assembly and expression of blood clotting enzyme complexes" <i>Annu Rev Biochem.</i> 57:915-56 (1988)	
104.	Martin et al. "Warfarin-resistance genotype determination in the Norway rat, <i>Rattus norvegicus</i> " <i>Laboratory Animals</i> 13:209-214 (1979)	
105.	Massari et al. "Helix-Loop-Helix Proteins: Regulators of Transcription in Eucaryotic Organisms" <i>Molecular and Cellular Biology</i> 20(2):429-440 (2000)	
106.	McGraw et al. "Evidence for a prevalent dimorphism in the activation peptide of human coagulation factor IX" <i>Proc. Natl. Acad. Sci. USA</i> 82:2847-2851 (1985)	
107.	McManus et al. "Gene Silencing in Mammals by Small Interfering RNAs" <i>Nature Reviews</i> 3:737-747 (2002)	
108.	McMillan et al. "Congenital Combined Deficiency of Coagulation Factors II, VII, IX, and X" <i>Medical Intelligence</i> 274(23):1313-1315 (1966)	
109.	Moor et al. "Coagulation Factor VII Mass and Activity in Young Men With Myocardial Infarction at a Young Age" <i>Arteriosclerosis, Thrombosis, and Vascular Biology</i> 15:655-664 (1995)	

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110.	Morris et al. "Processive Post-translational Modification" <i>The Journal of Biological Chemistry</i> 270(51):30491-30498 (1995)	
111.	Morris et al. "Characterization of the Purified Vitamin K-dependent $\gamma$ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 268(12):8735-8742 (1993)	
112.	Morrissey et al. "Quantitation of Activated Factor VII Levels in Plasma Using a Tissue Factor Mutant Selectively Deficient in Promoting Factor VII Activation" <i>Blood</i> 81(3):734-744 (1993)	
113.	Mumberg et al. "Regulatable promoters of <i>Saccharomyces cerevisiae</i> : comparison of transcriptional activity and their use for heterologous expression" <i>Nucleic Acids Research</i> 22(25):5767-5768 (1994)	
114.	Mukharji et al. "Purification of a vitamin K epoxide reductase that catalyzes conversion of vitamin K 2,3-epoxide to 3-hydroxy-2-methyl-3-phytyl-2,3-dihydronaphthoquinone" <i>Proc. Natl. Acad. Sci. USA</i> 82:2713-2717 (1985)	
115.	Mutero et al. "Resistance-associated point mutations in insecticide-insensitive acetylcholinesterase" <i>Proc. Natl. Acad. Sci.</i> 91:5922-5926 (1994)	
116.	Mutucumarana et al. "A Conserved Region of Human Vitamin K-dependent Carboxylase Residues 393 and 404 is Important for Its Interaction with the Glutamate Substrate" <i>The Journal of Biological Chemistry</i> 278:46488-46493 (2003)	
117.	Mutucumarana et al. "Expression and Characterization of the Naturally Occurring Mutation L394R in Human $\gamma$ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 275(42):32572-32577 (2000)	
118.	Nellen et al. "What makes an mRNA anti-sense-itive" <i>TIBS</i> 18:419-423 (1993)	
119.	Nelsestuen et al. "Role of $\gamma$ -Carboxyglutamic Acid" <i>The Journal of Biological Chemistry</i> 251(22):6886-6893 (1976)	
120.	Nelsestuen et al. "The Mode of Action of Vitamin K" <i>The Journal of Biological Chemistry</i> 249(19):6347-6350 (1974)	
121.	Oldenburg et al. "Congenital Deficiency of Vitamin K Dependent Coagulation Factors in Two Families Presents as a Genetic Defect of the Vitamin K-Epoxide-Reductase-Complex" <i>Thromb Haemost</i> 84:937-941 (2000)	
122.	O'Reilly et al. "Hereditary Transmission of Exceptional Resistance to Coumarin Anticoagulant Drugs" <i>The New England Journal of Medicine</i> 271:809-815 (1964)	
123.	O'Reilly et al. "The Second Reported Kindred With Hereditary Resistance to Oral Anticoagulant Drugs" <i>The New England Journal of Medicine</i> 282:1448-1451 (1970)	
124.	Pauli et al. "Association of Congenital Deficiency of Multiple Vitamin K-dependent Coagulation Factors and the Phenotype of the Warfarin Embryopathy: Clues to the Mechanism of Teratogenicity of Coumarin Derivatives" <i>Am. J. Hum. Genet.</i> 41:566-583 (1987)	
125.	Petersen et al. "Probing the Structure of the Warfarin-Binding Site on Human Serum Albumin Using Site-Directed Mutagenesis" <i>Proteins</i> 47:116-125 (2002)	
126.	Presnell et al. "The Vitamin K-dependent Carboxylase" <i>Thromb Haemost</i> 87:937-946 (2002)	
127.	Presnell et al. "A Novel Fluorescence Assay To Study Propeptide Interaction with $\gamma$ -Glutamyl Carboxylase" <i>Biochemistry</i> 40:11723-11733 (2001)	
128.	Price "Role of Vitamin-K-Dependent Proteins in Bone Metabolism" <i>Ann Rev Nutr</i> 8:565-583 (1988)	
129.	Rehemtulla et al. "In vitro and in vivo functional characterization of bovine vitamin K-dependent $\gamma$ -carboxylase expressed in Chinese hamster ovary cells" <i>Proc. Natl. Acad. Sci. USA</i> 90:4611-4615 (1993)	
130.	Rettie et al. "Hydroxylation of warfarin by human cDNA-expressed cytochrome P-450: a role for P-450C9 in the etiology of (S)-warfarin-drug interactions" <i>Chem Res Toxicol.</i> 5(1):54-59 (1992)	
131.	Rusconi et al. "RNA aptamers as reversible antagonists of coagulation factor IXa" <i>Nature</i> 419:90-94 (2002)	
132.	Russell et al. "Nucleotide Sequence of the Yeast Alcohol Dehydrogenase II Gene" <i>The Journal of Biological Chemistry</i> 258(4):2674-2682 (1983)	
133.	Scahill et al. "Expression and characterization of the product of a human immune interferon cDNA gene in Chinese hamster ovary cells" <i>Proc. Natl. Acad. Sci. USA</i> 80:4654-4658 (1993)	
134.	Seffernick et al. "Melamine Deaminase and Atrazine Chlorohydrolase: 98 Percent Identical but Functionally Different" <i>Journal of Bacteriology</i> 183(8):2405-2410 (2001)	
135.	Soute et al. "Characteristics of recombinant W501S mutated human $\gamma$ -glutamyl carboxylase" <i>Journal of Thrombosis and Haemostasis</i> 2:597-604 (2004)	

Examiner Signature		Date Considered	
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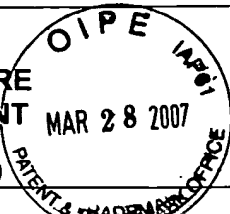
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		Application Number		10/573,131			
		Filing Date		April 18, 2006			
		First Named Inventor		Darrel W. Stafford			
		Group Art Unit		1634			
Examiner Name		J. Sitton		Attorney Docket Number		5470-401	
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136.	Sperling et al. "Metal Binding Properties of $\gamma$ -Carboxyglutamic Acid" <i>The Journal of Biological Chemistry</i> 253(11):3898-3906 (1978)	
137.	Spronk et al. "Novel mutation in the $\gamma$ -glutamyl carboxylase gene resulting in congenital combined deficiency of all vitamin K-dependent blood coagulation factors" <i>Blood</i> 96(10):3650-3652 (2000)	
138.	Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9923231; GenBank Accession No. NT_024812.10, November 5, 2003	
139.	Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NC_000016.5, August 10, 2004	
140.	Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NT_024812.10, March 19, 2004, Details: ss21323934	
141.	Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NT_024812.10, November 5, 2003, Details: ss13773513	
142.	Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs9934438; GenBank Accession No. NT_024812.10, February 20, 2004, Details: ss19348150	
143.	Single Nucleotide Polymorphism (SNP) RefSNP(rs#) rs8050394; GenBank Accession No. NT_010393, July 4, 2003	
144.	Single Nucleotide Polymorphism (SNP) RefSNP (rs#) rs8359612; GenBank Accession No. AACN010884940, September 14, 2003	
145.	Single Nucleotide Polymorphism (SNP) RefSNP (rs#) rs7294; GenBank Accession No. AA708782, August 23, 1999	
146.	Stafford et al. "The vitamin K cycle" <i>Journal of Thrombosis and Haemostasis</i> 3:1873-1878 (2005)	
147.	Stanley et al. "Amino Acids Responsible for Reduced Affinities of Vitamin K-Dependent Propeptides for the Carboxylase" <i>Biochemistry</i> 38:15681-15687 (1999)	
148.	Stanley et al. "Role of the Propeptide and $\gamma$ -Glutamic Acid Domain of Factor IX for <i>in Vitro</i> Carboxylation by the Vitamin K-Dependent Carboxylase" <i>Biochemistry</i> 37:13262-13268 (1998)	
149.	Stanley et al. "The Propeptides of the Vitamin K-dependent Proteins Possess Different Affinities for the Vitamin K-dependent Carboxylase" <i>The Journal of Biological Chemistry</i> 274:16940-16944 (1999)	
150.	Stein et al. "Antithrombotic therapy in patients with mechanical and biological prosthetic heart valves" <i>Chest</i> 108:371S-379S (1995)	
151.	Stenflo et al. "Vitamin K-dependent formation of gamma-carboxyglutamic acid" <i>Annu Rev Biochem.</i> 46:157-72 (1977)	
152.	Stitt et al. "The Anticoagulation Factor Protein S and Its Relative, Gas6, Are Ligands for the Tyro 3/Axl Family of Receptor Tyrosine Kinases" <i>Cell</i> 80:661-670 (1995)	
153.	Strausberg et al. "Generation and initial analysis of more than 15,000 full-length human and mouse cDNA sequences" <i>PNAS</i> 99(26):16899-16903 (2002)	
154.	Sun et al. "Vitamin K epoxide reductase significantly improves carboxylation in a cell line overexpressing factor X" <i>Blood</i> 106(12):3811-3815 (2005)	
155.	Terai et al. "Human homologue of maid: A dominantly inhibitory helix-loop-helix protein associated with liver-specific gene expression" <i>Hepatology</i> 32(2):357-66 (2000)	
156.	Tie et al. "Determination of Disulfide Bond Assignment of Human Vitamin K-dependent $\gamma$ -Glutamyl Carboxylase by Matrix-assisted Laser Desorption/Ionization Time-of-Flight Mass Spectrometry" <i>The Journal of Biological Chemistry</i> 278:45468-45475 (2003)	
157.	Tie et al. "A topological study of the human $\gamma$ -glutamyl carboxylase" <i>Blood</i> 96:973-978 (2000)	
158.	Tie et al. "Identification of the N-Linked Glycosylation Sites of Vitamin K-Dependent Carboxylase and Effect of Glycosylation on Carboxylase Function" <i>Biochemistry</i> 45:14755-14763 (2006)	
159.	Tie et al. "Chemical Modification of Cysteine Residues Is a Misleading Indicator of Their Status as Active Site Residues in the Vitamin K-dependent $\gamma$ -Glutamyl Carboxylation" <i>The Journal of Biological Chemistry</i> 279:54079-54087 (2004)	
160.	Tie et al. "Membrane Topology Mapping of Vitamin K Epoxide Reductase by <i>in Vitro</i> Translation/Cotranslocation" <i>The Journal of Biological Chemistry</i> 280:16410-16416 (2005)	
161.	Toomajian et al. "Sequence Variation and Haplotype Structure at the Human HFE Locus" <i>Genetics</i> 161:1609-1623 (2002)	
162.	Uhlmann et al. "Antisense Oligonucleotides: A New Therapeutic Principle" <i>Chemical Reviews</i> 90(4):543-584 (1990)	

Examiner Signature		Date Considered	
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Sheet	7 of 7	Attorney Docket Number	5470-401		

163.	Wajih et al. "Engineering of a Recombinant Vitamin K-dependent $\gamma$ -Carboxylation System with Enhanced $\gamma$ -Carboxyglutamic Acid Forming Capacity" <i>The Journal of Biological Chemistry</i> 280(11):10540-10547 (2005)
164.	Wajih et al. "The Inhibitory Effect of Calumenin on the Vitamin K-dependent $\gamma$ -Carboxylation System" <i>The Journal of Biological Chemistry</i> 279(24):25276-25283 (2004)
165.	Wajih et al. "Increased Production of Functional Recombinant Human Clotting Factor IX by Baby Hamster Kidney Cells Engineered to Overexpress VKORC1, the Vitamin K 2,3-Epoxy-reducing Enzyme of the Vitamin K Cycle" <i>The Journal of Biological Chemistry</i> 280(36):31603-31607 (2005)
166.	Wallace et al. "Hybridization of synthetic oligodeoxyribonucleotides to $\Phi$ x174 DNA: the effect of single base pair mismatch" <i>Nucleic Acids Research</i> 6(11):3543-3557 (1979)
167.	Wallin et al. "A molecular mechanism for genetic warfarin resistance in the rat" <i>The FASEB Journal</i> 15:2542-2544 (2001)
168.	Wallin et al. "Vitamin K-dependent Carboxylation and Vitamin K Metabolism in Liver" <i>J. Clin. Invest.</i> 76:1879-1884 (1985)
169.	Wang et al. "Identification of a gene encoding a typical $\gamma$ -carboxyglutamic acid domain in the tunicate <i>Halocynthia roretzi</i> " <i>Journal of Thrombosis and Haemostasis</i> 1:118-123 (2003)
170.	Ware et al. "Factor IX San Dimas" <i>The Journal of Biological Chemistry</i> 264(19):11401-11406 (1989)
171.	Wasley et al. "PACE/Furin Can Process the Vitamin K-dependent Pro-factor IX Precursor within the Secretory Pathway" <i>The Journal of Biological Chemistry</i> 268(12):8458-8465 (1993)
172.	Watzke et al. "Factor X Santo Domingo Evidence that the Severe Clinical Phenotype Arises from a Mutation Blocking Secretion" <i>J. Clin. Invest.</i> 88:1685-1689 (1991)
173.	Wells et al. "Additivity of Mutational Effects in Proteins" <i>Biochemistry</i> 29(37):8509-8517 (1990)
174.	Winter et al. "Man-made antibodies" <i>Nature</i> 349:293-299 (1991)
175.	Wu et al. "In Vitro $\gamma$ -Carboxylation of a 59-Residue Recombinant Peptide Including the Propeptide and the $\gamma$ -Carboxyglutamic Acid Domain of Coagulation Factor IX" <i>The Journal of Biological Chemistry</i> 265(22):13124-13129 (1990)
176.	Wu et al. "The Propeptide Binding Site of the Bovine $\gamma$ -Glutamyl Carboxylase" <i>The Journal of Biological Chemistry</i> 272:11718-11722 (1997)
177.	Wu et al. "Identification and purification to near homogeneity of the vitamin K-dependent carboxylase" <i>Proc. Natl. Acad. Sci. USA</i> 88:2236-2240 (1991)
178.	Xie et al. "Molecular basis of ethnic differences in drug disposition and response" <i>Annu Rev Pharmacol Toxicol.</i> 41:815-50 (2001)
179.	Zhang et al. "Role of Individual $\gamma$ -Carboxyglutamic Acid Residues of Activated Human Protein C in Defining its In Vitro Anticoagulant Activity" <i>Blood</i> 80(4):942-952 (1992)
180.	Zheng et al. "Inhibition of gene expression by anti-sense oligodeoxynucleotides" <i>Clin. Exp. Immunol.</i> 100:380-382 (1995)
181.	Zimmermann et al. "Biochemical Basis of Hereditary Resistance to Warfarin in the Rat" <i>Biochemical Pharmacology</i> 23:1033-1040 (1974)

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